

a²
contd

26. (amended) A pharmaceutical composition according to claim 23 wherein the β_3 agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

27. (amended) A pharmaceutical composition according to claim 23 containing from 0.5 to 600 mg of CB₁ receptor antagonist and from 0.5 to 600 mg of β_3 -agonist.

a³

32. (amended) A kit according to claim 31 in which said CB₁ receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates and said β_3 -agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

33. (amended) A kit according to claim 30 in which said active principles are in different packagings.

Please add the following new claim:

a⁴

39. (added) A pharmaceutical composition according to claim 26 wherein the CB₁ antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide or one of its pharmaceutically acceptable salts or one of their solvates.

REMARKS

The specification has been amended in order to provide the appropriate cross-reference to related application information.

Claims 1-18 and 34-38, which are directed to the subject matter which was elected for prosecution and allowed in U.S. application Serial No. 09/341,764, have been canceled.

Claims 19-27 and 32-33 have been rewritten in accordance with U.S. practice, and multiple dependencies have been eliminated from claims 21, 23-27 and 32-33.

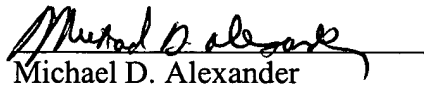
New claim 39 is directed to a pharmaceutical composition containing the preferred CB₁ antagonist and B₃ agonist recited separately in composition claims 22 and 26, respectively.

Claims 19-33 and 39 remain in the application

Attached hereto is a marked-up version of the changes made to the specification and claims by the instant amendment. The marked-up version is entitled "Version With Markings To Show Changes Made".

Respectfully submitted,

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Michael D. Alexander
Registration No. 36,080

Sanofi-Synthelabo Inc.
9 Great Valley Parkway
Malvern, PA 19355
Tel.: (610) 889-8802
Fax: (610) 889-8799

Version With Markings to Show Changes Made

In the specification

On page 1, after the title of the invention and before line 2 insert the following cross reference to related application section was inserted:

--Cross Reference to Related Applications

This application is a divisional of prior copending application, Serial No. 09/341,764, filed August 19, 1999, which in turn is a 35 U.S.C. 371 application of PCT International application No. PCT/FR98/00154, filed January 28, 1998, which in turn claims priority from French application No. 97/00870, filed January 28, 1997.--

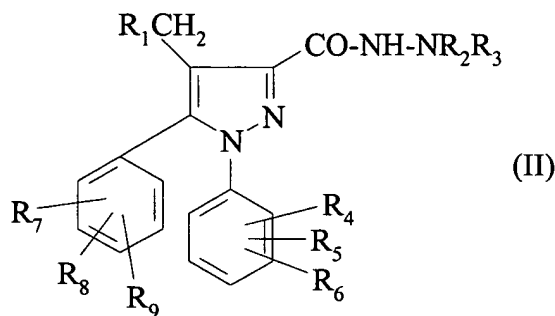
In the Claims:

Claims 19-27 and 32-33 have been amended as follows:

19. (amended) A pharmaceutical composition containing a CB₁ receptor antagonist and a regulator of metabolic functions together with a pharmaceutical excipient.

20. (amended) A pharmaceutical composition according to claim 19[, characterized in that] wherein said regulator of metabolic functions is a β_3 -agonist.

21. (amended) A pharmaceutical composition according to claim [19 or] 20[, characterized in that] wherein the CB₁ receptor antagonist is a compound of the formula



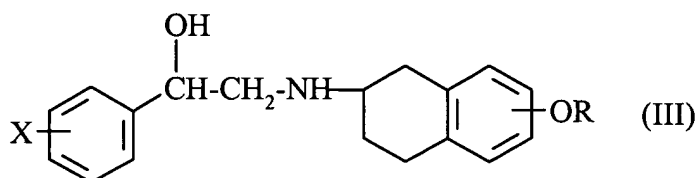
in which:

- R₁ is hydrogen, a fluorine, a hydroxyl, a (C₁-C₅)alkoxy, a (C₁-C₅)alkylthio, a hydroxy(C₁-C₅)alkoxy, a group -NR₁₀R₁₁, a cyano, a (C₁-C₅)alkylsulfonyl or a (C₁-C₅)alkylsulfinyl;

- R_2 and R_3 are a (C_1-C_4) alkyl or, together with the nitrogen atom to which they are bonded, form a saturated or unsaturated 5- to 10-membered heterocyclic radical which is unsubstituted or monosubstituted or polysubstituted by a (C_1-C_3) alkyl or by a (C_1-C_3) alkoxy;
 - R_4 , R_5 , R_6 , R_7 , R_8 and R_9 are each independently hydrogen, a halogen or a trifluoromethyl, and if R_1 is a fluorine, R_4 , R_5 , R_6 , R_7 , R_8 and/or R_9 can also be a fluoromethyl, with the proviso that at least one of the substituents R_4 or R_7 is other than hydrogen;
 - R_{10} and R_{11} are each independently hydrogen or a (C_1-C_5) alkyl, or R_{10} and R_{11} , together with the nitrogen atom to which they are bonded, form a heterocyclic radical selected from pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl and piperazin-1-yl, which is unsubstituted or substituted by a (C_1-C_4) alkyl,
- one of its salts or one of their solvates.

22. (amended) A pharmaceutical composition according to claim 21[, characterized in that] wherein the CB_1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates.

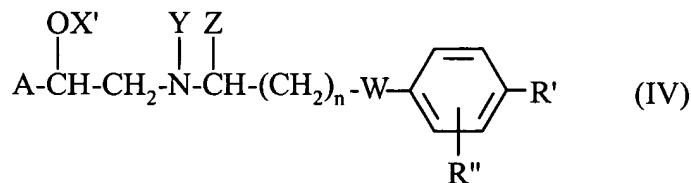
23. (amended) A pharmaceutical composition according to [any one of claims 20 to 22, characterized in that] claim 21 wherein the β_3 -agonist is a compound of the formula



in which:

- X is hydrogen, a halogen, a trifluoromethyl or a (C_1-C_4) alkyl;
 - R is hydrogen or a methyl which is unsubstituted or substituted by a carboxyl or an alkoxycarbonyl in which the alkoxy is (C_1-C_6) ,
- or one of its pharmaceutically acceptable salts.

24. (amended) A pharmaceutical composition according to [any one of claims 20 to 22, characterized in that] claim 21 wherein the β_3 -agonist is a compound of the formula



in which:

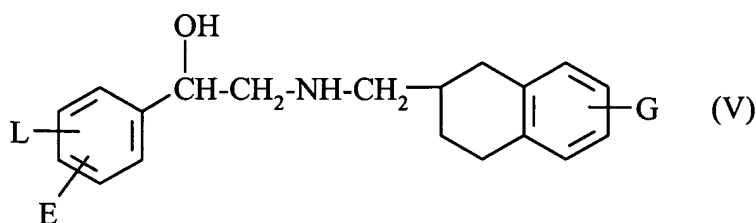
- n is 1, 2 or 3;
- A is a benzofuran-2-yl or a phenyl which is unsubstituted or substituted by one or two halogen atoms or by a (C₁-C₄)alkyl or a trifluoromethyl;
- R' is:
 - hydrogen;
 - a (C₁-C₆)alkyl;
 - a functional group selected from the following groups: hydroxyl; (C₁-C₆)alkoxy; (C₂-C₆)alkenyloxy; (C₂-C₆)alkynyloxy; (C₃-C₈)cycloalkoxy; (C₃-C₈)cycloalkyl(C₁-C₆)alkoxy; benzyloxy; phenoxy; mercapto; (C₁-C₆)alkylthio; (C₂-C₆)alkenylthio; (C₂-C₆)alkynylthio; (C₃-C₈)cycloalkylthio; (C₃-C₈)cycloalkyl(C₁-C₆)alkylthio; benzylthio; phenylthio; (C₁-C₆)alkylsulfinyl; (C₂-C₆)alkenylsulfinyl; (C₂-C₆)alkynylsulfinyl; (C₃-C₈)cycloalkylsulfinyl; (C₃-C₈)cycloalkyl(C₁-C₆)alkylsulfinyl; benzylsulfinyl; phenylsulfinyl; (C₁-C₆)alkylsulfonyl; (C₂-C₆)alkenylsulfonyl; (C₂-C₆)alkynylsulfonyl; (C₃-C₈)cycloalkylsulfonyl; (C₃-C₈)cycloalkyl(C₁-C₆)alkylsulfonyl; benzylsulfonyl; phenylsulfonyl; cyano; nitro; amino which is unsubstituted or substituted by one or two identical or different radicals selected from (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, (C₃-C₈)cycloalkyl(C₁-C₆)alkyl, benzyl and phenyl groups; carboxyl; alkoxycarbonyl in which the alkoxy is (C₁-C₆); (C₂-C₆)alkenyloxycarbonyl; (C₂-C₆)alkynyloxycarbonyl; (C₃-C₈)cycloalkoxycarbonyl; (C₃-C₈)cycloalkyl(C₁-C₆)alkoxycarbonyl; benzyloxycarbonyl; phenoxycarbonyl; and carbamoyl which is unsubstituted or

substituted on the amino group by one or two identical or different radicals selected from (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₃-C₈)cycloalkyl, (C₃-C₈)cycloalkyl(C₁-C₆)alkyl, benzyl and phenyl groups;

- a group R''' selected from the following groups: (C₁-C₆)alkyl substituted by a functional group; (C₂-C₆)alkenyl substituted by a functional group; (C₂-C₆)alkynyl substituted by a functional group; phenyl(C₁-C₆)alkyl substituted on the phenyl by a (C₁-C₆)alkyl or by a functional group; phenyl(C₂-C₆)alkenyl substituted on the phenyl by a (C₁-C₆)alkyl or by a functional group; phenyl(C₂-C₆)alkynyl substituted on the phenyl by a (C₁-C₆)alkyl or by a functional group; benzyl substituted on the phenyl by a (C₁-C₆)alkyl or by a functional group; and phenyl which is unsubstituted or substituted by a (C₁-C₆)alkyl or by a functional group, the functional group being as defined above;
- a group O-R''', S-R''', SO-R''' or SO₂-R''', in which R''' is as defined above;
- a group NR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group COOR''' or a group CO-SR''', in which R''' is as defined above;
- a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group SO₂NR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- R'' is hydrogen; a halogen; a (C₁-C₆)alkyl; a functional group as defined above; a group OR''', R''' being as defined above; a group COOR''', R''' being as defined above; or a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- W is a direct bond or an oxygen atom;
- X' is hydrogen, a (C₁-C₆)alkyl or a (C₁-C₆)alkylcarbonyl;

- Y is hydrogen or a group A'-CH(OH)-CH₂-, A' being identical to A but other than benzofuran-2-yl; or
 - X' and Y, taken together, form a methylene group optionally substituted by an alkoxy carbonyl in which the alkoxy is (C₁-C₆); an ethylene group optionally substituted by an oxo group; or a 1,3-propylene group;
 - Z is hydrogen or a (C₁-C₆)alkyl,
- or one of its pharmaceutically acceptable salts.

25. (amended) A pharmaceutical composition according to [any one of claims 20 to 22] claim 21 wherein the β_3 -agonist is a compound of the formula



in which:

- E is hydrogen, a (C₁-C₄)alkyl, a (C₁-C₄)alkoxy, a phenyl, a nitro, a halogen atom or a trifluoromethyl;
- L is hydrogen, a (C₁-C₄)alkyl, a (C₁-C₄)alkoxy, a phenyl, a nitro or a halogen atom; or E and L together are a group -CH=CH-CH=CH- or -CH₂-CH₂-CH₂-CH₂-; and
- G is hydrogen, a chlorine atom, a hydroxyl or a group OG', in which G' is a (C₁-C₄)alkyl which is unsubstituted or substituted by a hydroxyl, (C₁-C₄)alkoxy, (C₁-C₄)alkoxycarbonyl, carboxyl or (C₃-C₇)cycloalkyl; a (C₃-C₇)cycloalkyl; or a (C₂-C₄)alkanoyl,

or one of its pharmaceutically acceptable salts.

26. (amended) A pharmaceutical composition according to claim 23[, characterized in that] wherein the β_3 agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

27. (amended) A pharmaceutical composition according to [any one of claims 20 to 26] claim 23 containing from 0.5 to 600 mg of CB₁ receptor antagonist and from 0.5 to 600 mg of β_3 -agonist.

32. (amended) A kit according to claim [30 or] 31 in which said CB₁ receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates and said β_3 -agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

33. (amended) A kit according to [any one of claims 30 to 32] claim 30 in which said active principles are in different packagings.

Claims 1-18 and 34-38 have been canceled.

New claim 39 has been added.